IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Hassan et al.

Assignee: Banner Pharmacaps Inc. | Confirmation No. 6260

Application Serial No. 10/529,984 | Art Unit 1626

Filed: March 31, 2005 | Examiner: Shterengarts, Samantha L.

Attorney Docket No. B4700 597 US

For: ENTERIC PREPARATIONS

APPELLANTS' APPEAL BRIEF UNDER 37 C.F.R. § 41.37

Mail Stop Appeal Brief—Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Attention: Board of Patent Appeals and Interferences

Sir:

This appeal brief is submitted according to 37 C.F.R. § 41.37 in support of the Notice of Appeal filed in the above-captioned application on December 28, 2010.

I. REAL PARTY IN INTEREST—37 C.F.R. § 41.37(c)(1)(i)

The real party in interest in this appeal is the assignee, Banner Pharmacaps Inc., a Delaware corporation.

II. RELATED APPEALS AND INTERFERENCES—37 C.F.R. § 41.37(c)(1)(ii)

There are no other appeals or interferences known to Appellants, Appellants' legal representatives, or assignees that may be related to, directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS—37 C.F.R. § 41.37(c)(1)(iii)

Claims 20 and 24–40 are pending in the application, with claim 20 being the sole independent claim. Claims 20 and 24–40 stand rejected. The rejection of claims 20 and 24–40

is appealed. Claims 1–19 were canceled in an Amendment filed July 22, 2008. Claims 21–23 were canceled in an Amendment filed April 16, 2008. Appellants filed a Notice of Appeal on August 17, 2009 and an Appeal Brief on October 19, 2009. An Amended Appeal Brief was filed on December 7, 2009. Prior to review by the Board, the Examiner vacated the final Office Action mailed on May 19, 2009, reopened prosecution, and issued a new Office Action on March 16, 2010 that rejected claims 20 and 24–40. This Action was made final in an Office Action mailed October 5, 2010. The rejections alleged constitute the complete set of rejections applied to the application.

IV. STATUS OF AMENDMENTS—37 C.F.R. § 41.37(c)(1)(iv)

No amendments after final rejection have been requested or entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER—37 C.F.R. § 41.37(c)(1)(v)

The sole independent claim is claim 20, which specifies as follows:

20. An enteric soft capsule shell formed from a gel mass composition comprising:
    (a) a film-forming, water-soluble polymer,
    (b) an acid-insoluble polymer; and
    (c) an alkaline aqueous solvent;
    wherein the ratio of acid-insoluble polymer to film-forming, water-soluble polymer is from 30:70 to 45:55 by weight;
    the final pH of the gel mass is less than or equal to about 9 pH units; and
    the moisture content of the enteric soft capsule shell formed from the gel mass composition is from about 2% to about 10%.

All dependent claims ultimately depend from claim 20. Accordingly, all claims are directed to an enteric soft capsule shell formed from a gel mass composition (*see at least* p. 3, ll. 28–29 of Appellants' originally filed application) comprising (a) a film-forming, water-soluble polymer (*see* p. 3, ll. 26–27); (b) an enteric acid-insoluble polymer (*see* p. 3, ll. 26–27), and (c) an alkaline aqueous solvent (*see* p. 4, ll. 10–12). In the gel mass composition, the ratio of the acid-insoluble polymer to film-forming, water-soluble polymer is from 30:70 to 45:55 by weight (*see* p. 15, ll. 24–27). In addition, the final pH of the gel mass is less than or equal to about 9 pH units (*see* p. 6, ll. 29–30), and the moisture content of the shell is from about 2% to about 10%

(*see* p. 4, l. 29). The claimed invention provides a direct method for manufacturing enteric soft capsules without the need for coating the capsule with an enteric composition. Furthermore, the enteric soft capsule does not require metal-induced cross-linking to gain its enteric character.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL—37 C.F.R. § 41.37(c)(1)(vi)

The grounds for rejection to be reviewed on appeal are set forth in the final Office Action mailed October 5, 2010. All pending claims, i.e., claims 20 and 24–40, stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over eight combinations of references as set forth below:

1. Claims 20, 24–25, and 27–40 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over WO 01/24780 (Venkateswara), in view of U.S. Patent No. 6,331,316 (the Ullah patent), and U.S. Patent No. 4,816,259 (Matthews). *See* Office Action mailed October 5, 2010 at 2–4.
2. Claim 34[1] stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Venkateswara, in view of the Ullah patent and Matthews, further in view of U.S. Patent No. 4,500,453 (Shank). *See id.* at 4–5.
3. Claims 20, 24–25, and 27–40 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Venkateswara, in view of U.S. Patent Application Publication No. 2001/0051188 (the Ullah publication), and Matthews. *See id.* at 5–6.
4. Claim 34[1] stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Venkateswara, in view of the Ullah publication and Matthews, further in view of Shank. *See id.* at 7.
5. Claims 20, 24–25 and 27–40 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 4,138,013 (Okajima) in view of the Ullah publication, and Matthews. *See id.* at 7–9.
6. Claim 34[1] stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Okajima in view of the Ullah publication and Matthews, and further in view of Shank. *See id.* at 9.

[1] Although the Examiner has rejected "claim 34," the rejection appears to have been directed to claim 26. This mistake is made throughout the October 5, 2010 Office Action and in previous Office Actions.

7. Claims 20, 24–25 and 27–40 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Okajima in view of the Ullah patent, and Matthews. *See id.* at 10–11.
8. Finally, claim 34[1] stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Okajima in view of the Ullah patent and Matthews, and further in view of Shank. *See id.* at 11–12.

VII. ARGUMENT—37 C.F.R. § 41.37(c)(1)(vii)

As set forth below, Appellants believe that the Examiner has not established a *prima facie* case of obviousness regarding any of the pending claims. In addition, or alternatively, even if the Examiner has established a *prima facie* case of obviousness (which Appellants hereby disaffirm), Appellants' arguments rebut *prima facie* obviousness.

A. Summary of the Law

The burden is on the Examiner to make a *prima facie* case of obviousness, which requires an objective analysis set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). *See also* the Examination Guidelines Update: Developments in the Obviousness Inquiry After *KSR v. Teleflex*, 75 Fed. Reg. 53643-53660 (Sept. 1, 2010), and the U.S. Patent & Trademark Office, Manual of Patent Examining Procedure, 8th ed., Revision 8 ("MPEP") at § 2142 (the "Examination Guidelines"). The *Graham* analysis includes: (1) determining the scope and content of the prior art; (2) ascertaining the differences between the claimed invention and the prior art; and (3) resolving the ordinary level of skill in the pertinent art. In addition to the factors cited above, the following criteria must be met in order to establish a proper *prima facie* case of obviousness: (1) the prior art reference (or references, when combined) must teach or suggest all the claim limitations; (2) the reference or combination of references must teach the predictable use of prior art elements according to their established functions; and (3) there must be a reasonable expectation of success in combining the teachings of the references. *Id.* In addition, the Examiner must also consider objective evidence that rebuts any assumption of predictability and reasonable expectation of success. *Id.* The obviousness analysis must be explicit and cannot be supported by mere conclusory statements. *Id.* Even if all elements of a claim may individually be found in various cited references, the proper standard for establishing *prima facie* obviousness requires *predictability in the art* and a *reasonable expectation of success*

when references are combined. As shown below, the Examiner has not established a *prima facie* case of obviousness under 35 U.S.C. § 103(a) and her assertions do not comport with the Examination Guidelines. Accordingly, the rejection of claims 20 and 24–40 should be reversed.

B. Rebuttal of the Examiner's Alleged *Prima Facie* Cases of Obviousness

1. Venkateswara, in view of the Ullah patent, and Matthews

The Examiner alleged that claims 20, 24–25, and 27–40 are unpatentable under 35 U.S.C. § 103(a) over Venkateswara, in view the Ullah patent and Matthews. *See* Office Action mailed October 5, 2010 at 2–4.

a. The Examiner has failed to establish a prima facie case of obviousness against claim 20

(i) The references do not teach all the elements of claim 20, such as the claimed ratio of polymers.

The invention of claim 20 is an enteric soft capsule shell formed from a gel mass having a specified composition. In particular, the claimed gel mass comprises a film-forming, water-soluble polymer, an acid-insoluble polymer; and an alkaline aqueous solvent. The claimed ratio of acid-insoluble polymer to film-forming, water-soluble polymer is from 30:70 to 45:55 by weight. The final pH of the gel mass is less than or equal to about 9 pH units and the moisture content of the enteric soft capsule shell formed from the gel mass composition is from about 2% to about 10%. The Examiner alleged that Venkateswara teaches an enteric soft capsule shell formed from a gel mass composition comprising a film-forming, water-soluble polymer, including gelatin, an acid-insoluble polymer, including hydroxypropyl methylcellulose phthalate, and an alkaline aqueous solvent and that the acid-insoluble polymer can be 40% by weight of the dried shell. *Id.* at 3. The Examiner admitted that Venkateswara is silent on the pH and water content of the composition. *Id.*

As Appellants discuss in detail below, Venkateswara does not disclose the claimed ratio of acid-insoluble polymer to film-forming, water-soluble polymer; however, the Examiner asserted that:

> Venkateswara et al. discloses the acid-insoluble polymer can be 40% by weight of the dried shell (pg. 5, lines 25–27). Given this disclosed weight percent of acid-insoluble polymer therefore, it can be concluded that the remaining polymer is present at a ratio of 30:70 (42%).

Id. The excerpt of Venkateswara cited above describes "a preferred embodiment" as follows: "The amount of such enteric polymer employed may range from 5.0–40.0 percent, preferably 5.0–25.0 percent by weight with reference to the ***dried shell***." *See* Venkateswara, at 5, ll. 25–27 (emphasis added). Contrary to the Examiner's assertion, this does not teach or suggest a ratio *of acid-insoluble polymer to film-forming polymer* as specified in Appellants' claims. Rather it teaches the ratio of acid-insoluble (enteric) polymer *to the entire composition of the dried shell*. The shell may (and in fact, according to Venkateswara, does) contain other ingredients such as glycerol and water. Thus, drying the shell changes the ratio of the acid-insoluble polymer with reference to the entire shell composition. Appellants' ratio of acid-insoluble polymer to film-forming polymer does not so change with drying the shell composition or with the addition of other shell ingredients. Even if the Examiner alleged that Venkateswara *inherently* teaches Appellants' claimed ratio of acid-insoluble polymer to film-forming polymer, such an allegation is unsupported because nowhere does Venkateswara teach or suggest any amounts of enteric acid-insoluble polymer and film-forming polymer that, if presented as a ratio, fall within the variable range claimed by Appellants. "The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient" for inherency. *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q. 2d 1949, 1950-51 (Fed. Cir. 1999) (emphasis added).

Furthermore, the Examiner's reasoning is flawed because it presumes that **every component** of the ***dried shell*** other than the "enteric polymer" would be a "film-forming polymer" such as gelatin. Based on this assumption, the Examiner asserted that, "it can be concluded that the remaining polymer is present at a ratio of 30:70 (42%)." Office Action mailed October 5, 2010 at 3. This assertion is wholly unsupported in Venkateswara, for at least the reason that the cited passage provides no information on the ***other components*** or ***total composition*** of the dried shell. Note that the dried shell mass includes the weight of plasticizers such as glycerol, solvent components such as buffers, and salts and other non-fugitive (i.e., unable to evaporate) components. In fact, just below the passage cited by the Examiner, Venkateswara specifically teaches that the gel mass (containing dry components and liquids) can contain preservatives, colorants, opacifiers, flavors, alkali metal salts, cross linking agents, benzimidazole, hydrophobic oily materials, buffering materials, thickeners, solubilizing or dispersing agents, and surface active agents. *See* Venkateswara at 5–7. Indeed, Venkateswara's Examples expressly teach the presence of additional ingredients such as glycerol. *Id.* at 8–17.

Such components would intrinsically change the weight percentages of the acid-insoluble polymer, the film-forming polymer, and the total weight of the gel mass and dried shell. Furthermore, Venkateswara's gel mass is dried under vacuum to produce the "dried shell." *See id.* at 8, Example 1, and *passim*. As such, the ratio of the dried shell cannot be extrapolated to a ratio in Appellants' claimed gel mass formulation (which is not dry) because the non-fugitive components inherently contribute to the mass of the dried shell.

Although Venkateswara **does not teach the claimed ratio**, Appellants have taken Venkateswara's raw mass values and converted them to mass : mass ratios for the sole purpose of rebutting the Examiner's arguments and to demonstrate that Appellants' claimed composition is outside the ranges allegedly taught by Venkateswara. *See* Table 1, shaded row, below.

Table 1: Appellants' Examples and Claimed Ratio of Acid-insoluble (Enteric) Polymer to Film-forming Polymer Compared with Venkateswara's Examples

Appellants' Examples, Claim 20	**Acid-insoluble / Total Dry Weight = Dry Weight %**	**Calculated Ratio: Acid-insoluble : Film-forming**
1, 8	9/45 = 20%	9 : 36 (20 : 80) = 0.25
13	13.5/45 = 30%	13.5 : 31.5 (30 : 70) = 0.43
24	18/45 = 40%	18 : 27 (40 : 60) = 0.67
Claim 20: (30:70–45:55)	13.5/45 = 30% 20.25/45 = 45%	13.5 : 31.5 (30 : 70) = 0.43 20.25 : 24.75 (45 : 55) = 0.82
	Dry Weight % Range: 20–45%	**Ratio Range: 0.25–0.82**
Venkateswara Examples	**Acid-insoluble / Total Dry Weight = Dry Weight %**	**Calculated Ratio: Acid-insoluble : Film-forming**
3	5/45 = 11.1%	5 : 40 = 0.125
10	7.5/47.5 = 15.8%	7.5 : 40 = 0.19
1, 4, 7, 8	7.5/42.5 = 17.6%	7.5 : 35 = 0.21
5	10/45 = 22.2%	10 : 35 = 0.28
2, 6, 9	10/40 = 25%	10 : 30 = 0.33
	Dry Weight % Range: 11–25%	**Ratio Range: 0.125–0.33**
Overlap	**20–25%**	**0.25–0.33**

Having converted the mass values of Venkateswara to ratios of enteric acid-insoluble polymer to film-forming polymer, it is apparent that no such converted ratio exceeds 10:30 (whole number: 0.33), compared to 30:70 (whole number: 0.43), which is the lowest end of the ratio range claimed by the Appellants. *See* Table 1. The converted Venkateswara ratios *are completely outside the range claimed by the Appellants*. While there is overlap between Venkateswara and the lower end of Appellants' **disclosed** (but not claimed) range, the ratio range specified in claim 20 lies completely outside any range taught by Venkateswara (*compare* Appellants' Examples 1 and 8, *with* Venkateswara's Examples 2, 6, and 9 in Table 1).

Moreover, it is notable that the term "ratio" is not used in the Venkateswara reference at all, and especially not to define the importance of a ratio of enteric acid-insoluble polymer to film-forming polymer. Consequently, Venkateswara fails to teach, suggest, or motivate the ratio of enteric acid-insoluble polymer to film-forming polymer specified in Appellants' claim 20.

Further, Venkateswara also fails to teach at least the following elements of claim 20:

- that the pH of the gel mass is less than or equal to pH 9 and;
- that the moisture content of the enteric soft capsule shell formed from the gel mass composition is from about 2% to about 10%.

Thus, the Examiner has misinterpreted the teachings of Venkateswara, after learning from Appellants' of the importance, and used hindsight to assert that this reference teaches a ratio of enteric polymer to film-forming water-soluble polymer. Such hindsight is **impermissible**. Without Appellants' application teaching a ratio of acid-insoluble polymer to film-forming polymer, the Examiner would not have been motivated to make the conversions. As discussed above, Venkateswara contains no teaching of the claimed ratio of enteric acid-insoluble polymer to film-forming polymer.

The secondary references, the Ullah patent, and Matthews (which are discussed in more detail below) are not cited for any teachings that cure the deficiencies of Venkateswara, especially with respect to the claimed ratio of polymers. The Ullah patent is cited for the alleged teaching relating to the pH of the gel mass. Matthews is cited for the alleged teaching that enteric soft capsule shells to have a moisture content of 8–10%. Because neither the Ullah patent nor Matthews teaches a ratio of enteric acid-insoluble polymer to film-forming water-soluble polymer, these secondary references fail to cure the noted deficiencies of Venkateswara.

Accordingly, a *prima facie* case of obviousness has not been established because the combination of these references does not teach all the elements of the claimed invention. Consequently, the rejection of claim 20 is in error and must be reversed.

(ii) Appellants have established criticality for the claimed range.

Appellants can also refute a *prima facie* case of obviousness based on ranges by showing the criticality of the claimed range. *See* MPEP § 2144.05(III). Appellants' have shown that ratios of enteric acid-insoluble polymer to film-forming polymer lower than the claimed ratio produced "border quality" compositions (i.e., 80:20; 0.25). *See* Appellant's Application, at 15,

ll. 22–29. Thus, the converted ratios of enteric acid-insoluble polymer to film-forming polymer of Venkateswara would not produce acceptable capsules. *See* Table 1, above, particularly Venkateswara's Examples 1, 3, 4, 7, 8, and 10. The lower limit of the range of the ratio of enteric acid-insoluble polymer to film-forming polymer in the composition **disclosed** by Appellants is the critical limit. Furthermore, the portion of the range allegedly overlapping with Venkateswara is a **disclosed** range and not the range **claimed** by Appellants. In claim 20, Appellants have specified an enteric soft capsule with a ratio of acid-insoluble polymer to film-forming polymer of 30:70 (0.43) to about 45:55 (0.82) where the final pH of the gel mass is less than or equal to about pH 9 and with a moisture content from about 2–10%. All of the elements of the claimed composition are interdependent and must be considered together for imparting the specified enteric characteristic. Accordingly, this evidence of advantageous properties empirically determined by the Appellants further rebuts the Examiner's alleged *prima facie* case of obviousness.

(iii) The secondary references are not relevant to intrinsically enteric soft capsule shell compositions.

The secondary references relied on by the Examiner are of questionable relevance to Appellants' invention. Thus, the Examiner's asserted arguments supporting the combination of the references have no relevance to Appellant's claimed composition. The secondary references do not relate to soft capsule shell compositions that are enteric without requiring additional enteric coatings. For example, the Ullah patent is of questionable relevance to Appellants' invention because the Ullah patent teaches **enteric *coatings* for tablets** (i.e., a hard tablet is coated with an enteric coating). Thus, this reference is inapplicable to **enteric *soft capsules***.

Matthews teaches an **enteric *coating* for gelatin capsules** (i.e., the capsule is made first, and then coated with an enteric composition). In contrast, Appellants' claimed invention is an **enteric soft capsule** that is "enteric" due to its composition and not owing to an **enteric coating** deposited thereon. The properties taught by Matthews are different for at least the reason that the Matthews coating must adhere to the surface of the gelatin capsule. In the claimed invention, the soft capsule ***shell*** (i.e., outer layer of the capsule) itself has enteric properties **without requiring a coating**. The alleged teaching of Matthews regarding moisture content applies to non-enteric soft gelatin capsules that are *coated* by an enteric coating to render them enteric.

Accordingly, the asserted motivation for modifying the moisture content is irrelevant because, for instance, Appellants' claimed enteric soft capsule shells do not require further processing to become "enteric."

(iv) There is no predictability or reasonable expectation of success achieved by combining the asserted references.

A further flaw in the Examiner's reasoning is that she presumes that combining the independent references will yield predictable and successful results. The Examiner alleged:

> It would have been prima facie obvious to one of ordinary skill in the art to increase the pH of the enteric soft capsule taught by Venkateswara et al. One would have been motivated to do so because Ullah et al. teaches that an increased pH provides a more stable composition for acid labile drugs which may be present the core [*sic*].

See Office Action mailed October 5, 2010 at 3. In another section, the Examiner alleged one ordinary having skill in the art would be "motivated to optimize the pH of the solution in order to maintain the active pharmaceutical ingredients in their desired salt form without any degradation of the active ingredients that may occur due to a change in pH." *See id.* at 4. These conclusory assertions are fallacious because there is no predictability or reasonable expectation of success achieved by combining these references.

The Ullah patent is relied on for teaching the pH of an enteric coating. The success of this alleged combination for an enteric soft capsule composition is *not predictable*, even if optimization is undertaken. Since the Ullah patent teaches the importance of pH in an enteric coating for tablets in view of the tablet core stability, it does not follow that combining Venkateswara with the Ullah patent would predictably lead to the claimed invention. The Ullah patent's teachings on the pH of enteric coatings for tablets are not predictably applicable to enteric soft capsules because the effect of the Ullah patent's pH on the enteric soft capsule composition cannot be ascertained without significant empirical experimentation. The factors influencing suitability for coating tablets are very different from the factors influencing suitability for soft capsules. For example, coated tablets are relatively rigid so that film brittleness may not be a large concern, but soft capsules must remain pliable and elastic.

Moreover, the asserted motivations for modifying the pH taught by Ullah are wholly unsupported by the references. The Ullah patent teaches pH adjustments of compositions

discussed therein to stabilize acid-labile drugs in the core of the tablet. Appellants' invention does not specify any features of acid-labile drugs in the core of the capsule for which the pH teachings of the Ullah patent would apply. Nor does the claimed invention specify any features of the salt forms of active ingredients. The claimed feature is that the pH of the gel mass is less than or equal to about pH 9. *See* Appellants' claim 20. In addition, Venkateswara also does not mention acid labile drugs or salt forms of active ingredients. Thus, the asserted motivation for combining the Ullah patent with Venkateswara is specious and unsupported.

Similarly with respect to Matthews, the Examiner asserted that "one would have been motivated to modify the moisture content to be between 8–10% in order to ensure the integrity of the enteric soft capsules given that enteric soft capsules are known to crack or undergo substantial deformation during . . . manufacturing . . . ." *See* Office Action mailed October 5, 2010 at 3. However, the considerations that apply to soft capsules are not identical to the considerations that apply to coatings for capsules. There is no reason to expect from Matthews that a particular moisture content should be used to make an enteric capsule shell itself, rather than a coating. Matthews applies a coating to an already made shell. Appellants' enteric compositions must be made into a shell. It cannot be predicted how the Matthews moisture composition would affect or interact the other elements of Appellants invention as claimed.

As above, the Examiner asserted that combining the teaching of Matthews with Venkateswara and the Ullah patent would predictably lead to the claimed invention. As shown, this assertion of combining claim elements to yield predictable properties by the "optimization of parameters" is unsupported by the references without significant empirical experimentation. Appellants' claimed gel mass is an interdependent composition such that variation of individual components may alter the claimed enteric properties. As such, the particular effects and success of altering the components or composition cannot be predicted.

Consequently, none of Venkateswara, the Ullah patent, or Matthews, independently or when combined, teach, suggest, or motivate the composition of the invention specified in claim 20 with any reasonable degree of predictability or success. Thus, the rejection of claim 20 as obvious over Venkateswara in view of the Ullah patent and Matthews is erroneous. This combination of references does not muster a *prima facie* case of obviousness for all the reasons set forth above. Furthermore, there is no reasonable rationale for combining these references to

arrive at the claimed invention with any degree of predictability or success. As such, the rejection must be reversed.

b. Claims 24–25 and 27–40

Claims 24–25 and 27–40 ultimately depend from claim 20. If an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. Thus, claims 24–25 and 27–40 are nonobvious for the reasons that claim 20 is not obvious over Venkateswara, in view of the Ullah patent, and Matthews. As discussed above, Venkateswara does not teach all the elements of independent claim 20. Further, the Examiner admitted that Venkateswara is silent on the pH and moisture content of the composition as applicable to independent claim 20. Moreover, as compared to the claimed invention, Venkateswara fails to teach at least the following with regard to the dependent claims:

- that the film-forming water-soluble polymer can be a carbohydrate selected from the group consisting of hydroxypropyl methylcellulose and methyl cellulose, as required by claim 28;
- that the ratio of plasticizer to film-forming, water-soluble polymer is from about 1:9 to about 1:1 by weight, as required by claim 39; and
- that the ratio of plasticizer to film-forming, water-soluble polymer is about 1:3 by weight, as required by claim 40.

Consequently, even if claim 20 was found unpatentable by the Board, claims 28, 39 and 40 would be patentably distinguishable as nonobvious over Venkateswara in view of the Ullah patent and Matthews.

The Examiner asserted that the Ullah patent teaches the pH of the gel mass. *See* Office Action mailed October 5, 2010 at 3. As discussed above, the Ullah patent does not teach pH adjustment for an enteric soft capsule and there would be no motivation to combine this reference with Venkateswara. Furthermore, the Ullah patent fails to teach at least the following dependent claims:

- that the alkaline aqueous solvent comprises an alkali selected from the group consisting of ammonia, sodium hydroxide, potassium hydroxide, ethylenediamine, hydroxylamine, and tri-ethanolamine, as required by claim 31;

- that the alkaline aqueous solvent comprises a volatile alkali, as required by claim 32;
- that the volatile alkali is selected from the group consisting of ammonia and ethylenediamine, as required by claim 33;
- that the alkaline aqueous solvent is a hydroalcoholic solution, as required by claim 34; and
- that the final pH of the gel mass is less than or equal to about 8.5, as required by claim 35.

Accordingly, even if claim 20 was found unpatentable by the Board, claims 31–35 would be patentably distinguishable as nonobvious over Venkateswara in view of the Ullah patent and Matthews.

Finally, the Examiner asserted that Matthews teaches that enteric soft capsule shells should have a moisture content of 8–10% and such capsules exhibit an improved mechanical strength and will not crack or undergo substantial deformation during manufacturing. *See* Office Action mailed October 5, 2010 at 3. However, Matthews fails to teach at least the following:

- that the enteric soft capsule shell has a moisture content from about 2% to about 10%, as required by claim 36;
- that the enteric soft capsule shell has a moisture content from about 4% to about 8%, as required by claim 37; and
- that the enteric soft capsule shell has a moisture content of about 8%, as required by claim 38.

As such, even if claim 20 was found unpatentable by the Board, claims 36–38 would be patentably distinguishable as nonobvious over Venkateswara in view of the Ullah patent and Matthews.

In summary, none of Venkateswara, the Ullah patent, or Matthews teach all the elements of claims 20, 24–25, and 27–40. Accordingly, this rejection is in error and must be reversed. Furthermore, even if independent claim 20 was found unpatentable by the Board, claims 28 and 31–40 would be patentably distinguishable as nonobvious over Venkateswara in view of the Ullah patent and Matthews because the claim elements iterated above are not taught by any combination of these references.

2. Venkateswara, in view of the Ullah patent, and Matthews, further in view of Shank

The Examiner alleged that "claim 34" is unpatentable over Venkateswara, in view of the Ullah patent and Matthews, further in view of Shank. *See* Office Action mailed October 5, 2010 at 4–5. Although the Examiner stated that "claim 34" is rejected, the actual rejection appears to be directed to claim 26, which specifies "about 100 to about 250 blooms." This error was pointed out to the Examiner during prosecution, but the Examiner failed to correct this evident mistake. The following remarks are directed to dependent claim 26.

Claim 25 depends from claim 20 and specifies that the "proteinaceous film-forming, water-soluble polymer" is gelatin. Claim 26 depends from claim 25 and specifies that the gelatin is "extracted from animal bones or skin, and has about 100 to about 250 blooms."

The Examiner cited Shank for the teaching that gelatin obtained from animal bones contains lower molecular weight fractions and enteric capsules made with gelatin having about 100 to about 250 blooms. However, Shank fails to teach at least that the proteinaceous film-forming, water-soluble polymer, **(a non-crosslinked)** gelatin, is extracted from animal bones or skins, and has about 100 to about 250 blooms. Shank teaches a range of 150–280 blooms for **cross-linked** gelatin compositions. The gelatin crosslinking is achieved by polyvalent metal ions such as alluminum. *See* Shank at col. 3, lines 4–30. Thus, Shank's teaching is inapplicable to claim 26 because such polyvalent metal cross-linked gelatin is not specified in the claims.

Furthermore, based at least on the remarks above in Sections 1(a)–(b) regarding the deficiencies of Venkateswara, the Ullah patent, and Matthews, the asserted teachings of Shank do not cure the deficiencies of the other references, as shown above. As such, the rejection is in error and must be reversed.

3. Venkateswara, in view of the Ullah publication, and Matthews

The Examiner alleged that claims 20, 24–25, and 27–40 are unpatentable over Venkateswara, in view of the Ullah publication, and Matthews. *See* Office Action mailed October 5, 2010 at 5–6. In view of the following remarks, these rejections should be reversed.

a. Claim 20

This rejection of claim 20 does not differ significantly from the rejection discussed above in Section 1(a) over the same references and based on the Ullah patent. The "Ullah publication,"

U.S. Patent Application No. 09/866,501, is a continuation-in-part application of U.S. Patent Application No. 09/549,455, which issued as U.S. Patent No. 6,331,316 (i.e., the Ullah patent). Thus, there are not significant differences in the two references (i.e., *tablets* are discussed in the Ullah patent and *beadlets* in the publication). Accordingly, it is not clear why the Examiner generated a multiplicity of rejections based on essentially the same reference. Nonetheless, the rejection of claim 20 should be reversed, at least in view of the foregoing and following remarks.

The Ullah publication discusses a high drug-load **spheronized beadlet** containing an acid labile drug and an **enteric coating** for such beadlet. *See* the Ullah publication, Abstract. The Examiner alleged that the Ullah publication teaches that the pH of an enteric coating polymer is raised using an alkalizing agent like sodium hydroxide and that the pH is raised to a point below the pH wherein the enteric integrity of the polymer could be lost. Allegedly, this partial acid neutralization provides a more stable composition for the acid labile drug in the beadlet core. *Id.* In this regard, Appellants refer to their remarks above in Section 1(b) with regard to the Ullah patent, the failure of the Ullah patent to cure the deficiencies of Venkateswara, the inapplicability of Ullah's pH teaching to soft capsule compositions that do not require a coating to become enteric, and the unpredictability of the art. In addition, there is no mention of acid labile drugs in the core of Appellants' claimed composition. As such, Appellants' remarks regarding the rejection over Venkateswara, in view of the Ullah patent and Matthews, provided above in Sections 1(a)–(b), traverse the asserted basis for this rejection. Accordingly, the rejection is in error and must be reversed.

b. Claims 24–25 and 27–40

As discussed above in Sections 1(a)–(b), and 3(a), Venkateswara, the Ullah publication, and Matthews do not render claim 20 obvious. If an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. Thus, claims 24–25 and 27–40 are nonobvious for the reasons that claim 20 is not obvious over Venkateswara, in view of the Ullah publication, and Matthews. In addition, given that the essential teachings of the Ullah patent and the Ullah publication are the same, the arguments and deficiencies set forth in Section 1(b) apply to traverse this rejection as well. For brevity, these arguments are not restated here. Accordingly, this rejection is in error and must be reversed.

4. Venkateswara, in view of the Ullah publication and Matthews, further in view of Shank

The Examiner alleged that claim 34 [i.e., claim 26] is unpatentable over Venkateswara, in view of the Ullah publication and Matthews, further in view of Shank. *See* Office Action mailed October 5, 2010 at 7. This rejection is traversed. The rejection is substantially the same as the rejection traversed in Section 2, based on the same references except, there, the Ullah patent is cited, and here, the published Ullah application is cited. As noted, the Ullah patent and the Ullah publication contain essentially the same teachings except that the Ullah publication refers to enteric-coated beadlets. Accordingly, for the reasons discussed above in Section 1(b) and 2(a), the rejection is in error and must be reversed.

5. Okajima, in view of the Ullah publication, and Matthews

The Examiner alleged that claims 20, 24–25, and 27–40 are unpatentable over Okajima, in view of the Ullah publication and Matthews. Office Action mailed October 5, 2010 at 7–9. In view of the following remarks, the rejection should be reversed.

As an initial matter, it is troubling, but telling that the Examiner has merely cut and pasted the *verbatim assertions of obviousness* for the Okajima reference as those used with respect to the Venkateswara reference *without bothering to change the name of the reference* (*compare* page 8, fourth ¶ and page 10, last ¶, *with* page 3, fifth ¶ and page 6, second ¶ of the Office Action mailed October 5, 2010). This error first appeared in the Office Action mailed March 16, 2010. However, the error was not corrected in the Office Action mailed October 5, 2010, *even after having been pointed out by the Appellants*. Such apathy is indicative of the unsubstantiated and conclusory allegations of obviousness and the lack of the required explicit analysis in support of a *prima facie* obviousness assertion. Regardless, as illustrated below, Okajima does not teach or suggest the asserted elements of Appellants' claimed invention. As such, the rejection is in error and should be reversed.

a. Claim 20

Okajima allegedly teaches **hard shell** pharmaceutical **capsules** with enteric properties formed by **dip molding**. *See* Okajima, *Abstract*. In other words, a hard shell capsule is dipped into an enteric coating to form the outer enteric coating for the capsule. *See* Okajima, col. 3, ll.

12–40. The Examiner asserted that the Okajima reference teaches a gel mass composition comprising a film-forming, water-soluble polymer, an acid-insoluble polymer, an alkaline aqueous solvent, and optionally, a plasticizer and a coloring agent. The Examiner admitted that Okajima does not teach a final pH of less than or equal to about 9 pH units and that the moisture content of the gel mass is from about 2% to about 10%. *See* Office Action mailed October 5, 2010 at 8.

The Examiner alleged, "Okajima et al. illustrates in Example 2 the ratio of acid-insoluble polymer to film-forming polymer being 50:50." *Id.* The relevant sentence of Example 2 reads, "[c]ellulose acetate phthalate (CAP, 50 g) is dissolved in 220 ml. of 1.5% aqueous ammonium hydroxide and 50 g of hydroxypropyl methylcellulose is added thereto." *See* Okajima, col. 5, ll. 57–60. The Examiner alleged that this sentence teaches a ratio of 50:50 (whole number: 1.0). However, Appellants' claimed ratio of the acid-insoluble polymer to film-forming polymer is not expressly or impliedly taught or suggested by Okajima. Furthermore, this "converted ratio" is significantly higher than the maximum specified ratio in Appellants' claimed range (i.e., 1.0 > 0.82). Accordingly, Okajima does not teach or suggest any "converted ratio" within Appellants' claimed range. As with Venkateswara, the claimed ratio of acid-insoluble polymer to film-forming polymer is not taught by Okajima.

What is further significant is that in Okajima, col. 3, ll. 64–67, a ratio of ammonium salt to gelatin (film-forming polymer) is specified: "The ratio of ammonium salt to gelatin or HPMC can be varied and is preferably 5 parts of ammonium salt by weight, measured as free acid form, to 1 to 5 parts by weight of gelatin or HPMC." No other ratios are mentioned in this patent. Under the construction doctrine of *expressio unius est exclusio alterius* (i.e., the express mention of one item or thing excludes all others), **the claimed ratio cannot be inferred or implied** from this reference. The authors of this patent expressly used a ratio to describe the relative amounts of gelatin and ammonium salts. Accordingly, they could have also used ratios to express the relative portions of acid-insoluble polymers to film-forming polymers, ***but they did not***. Consequently, the claimed ratio of acid-insoluble polymer to film-forming polymer cannot be inferred from the teachings of Okajima, because the authors did not intend this to be a ratio.

Furthermore, the Examiner's conversion of the weights to ratios of acid-insoluble polymer to film-forming polymer as discussed above uses **impermissible hindsight**. Without Appellants' teaching, the Examiner would not have been motivated to make the ratio conversion.

Moreover, Okajima fails to teach at least the following elements of claim 20:

- a ratio of acid-insoluble polymer to film-forming, water-soluble polymer from 30:70 to 45:55 by weight;
- that the pH of the gel mass is less than or equal to pH 9; and
- that the moisture content of the enteric soft capsule shell formed from the gel mass composition is from about 2% to about 10%.

Accordingly, Okajima fails to teach or suggest the composition in claim 20 and neither secondary reference, Matthews or the Ullah publication, independently or in combination, cures the deficiencies of Okajima. *See* the discussion in Sections 1(a)–(b), above. For at least these reasons, no *prima facie* case of obviousness has been established. Consequently, the rejection is in error and must be reversed.

b. Claims 24–25 and 27–40

Claim 20 is the sole independent claim and claims 24–25 and 27–40 ultimately depend from claim 20. As discussed above in Sections 5(a), 3(a), 3(b), 1(a), and 1(b), Okajima, the Ullah publication, and Matthews do not teach all the elements of claim 20. If an independent claim is nonobvious, then any claim depending therefrom is nonobvious. Okajima does not cure any of the deficiencies described above with regard to Venkateswara or the other asserted references. Thus, claims 24–25 and 27–40 are nonobvious for the reasons that claim 20 is not obvious over Okajima, in view of the Ullah publication, and Matthews, and further in view of the arguments set forth in Sections 5(a), 3(a)–(b), and 1(a)–(b) with respect to these dependent claims (and Venkateswara instead of Okajima). Accordingly, this rejection is erroneous and must be reversed. Furthermore, even if independent claim 20 was found unpatentable by the Board, claims 28 and 31–40 would be patentably distinguishable as nonobvious over Okajima in view of the Ullah publication and Matthews because the claim elements iterated above in Section 1(b) are not taught by any combination of these references.

6. Okajima, in view of the Ullah publication, and Matthews, further in view of Shank

The Examiner alleged that claim 34 [claim 26] is unpatentable over Okajima, in view of the Ullah publication and Matthews, further in view of Shank. *See* Office Action mailed October 5, 2010 at 9. This rejection is traversed in view of the substantially similar rejection above in

Section 4, based on the same secondary references and Venkateswara. As discussed above in Sections 5(a)–(b), Okajima does not teach all the elements of claim 20, and 24–25, and 27–40. The Ullah publication and Matthews, further in view of Shank do not cure the deficiencies of Okajima. Appellants' arguments with respect to Shank as set forth in Section 2 apply to this rejection as well and, for the sake of brevity, are not repeated here. Accordingly, the rejection is in error and must be reversed.

7. Okajima, in view of the Ullah patent, and Matthews

The Examiner alleged that claims 20, 24–25, and 27–40 are unpatentable over Okajima, in view of the Ullah patent and Matthews. Office Action mailed October 5, 2010 at 10–11. In view of the following remarks, the rejection is traversed.

a. Claim 20

As above, with respect to the parallel rejection based on Venkateswara in Section 3, this rejection does not differ significantly from the similar rejection over the same references and based on the Ullah patent. There would not appear to be significant differences (beadlets discussed in the Ullah publication as compared to tablets discussed in the Ullah patent) in relation to the Examiner's assertions. Again, it is not clear why the Examiner has generated a multiplicity of rejections based on essentially the same cited disclosure applied against the same claims of the present application. In any event, the rejection is properly traversed, at least in view of the foregoing and the following remarks.

The Examiner's arguments based on alleged teachings of the Ullah patent, appearing at page 10 of the Office Action mailed October 5, 2010, are identical to those asserted on pages 5–6 of the Office Action regarding the rejection based on Venkateswara as primary reference. The Examiner's arguments concerning the asserted teachings of Matthews are also identical to those asserted in the rejection discussed above in Sections 1(a) and 1(b). Thus, no combination of the cited reference could construct Appellants' claimed invention, as discussed above. For at least these reasons, no *prima facie* case of obviousness has been established. Consequently, this rejection must be reversed.

b. Claims 24–25 and 27–40

As discussed above in Sections 7(a), and 1(a)–(b), Okajima, the Ullah patent, and Matthews do not teach all the elements of claim 20. *See* the discussion in Section 1(b), above regarding the deficiencies of these references. If an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious. Thus, claims 24–25 and 27–40 are nonobvious for the reasons that claim 20 is not obvious over Okajima, in view of the Ullah patent, and Matthews, and further in view of the arguments set forth above with respect to the dependent claims. Accordingly, these rejections are in error and must be reversed.

8. Okajima, in view of the Ullah patent, and Matthews, further in view of Shank

The Examiner alleged that claim 34 [claim 26] is unpatentable over Okajima, in view of the Ullah patent and Matthews, further in view of Shank. Office Action mailed October 5, 2010 at 11–12. This rejection is traversed in view of remarks above in Section 6 relating to the substantially similar rejection, based on the same references except citing the Ullah publication instead of the Ullah patent. The similarity of these two references has been previously discussed. Accordingly, the rejection is in error and must be reversed.

* * * * *

Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness with respect to claim 20 (and of claims 24–40 that depend from claim 20), or if established, Appellants have successfully refuted such a *prima facie* case as set forth above. Consequently, all asserted bases for rejection under 35 U.S.C. § 103(a) with respect to Venkateswara, Okajima, Matthews, the Ullah patent, the Ullah publication, and Shank are traversed. Accordingly, it is respectfully requested that the Board of Patent Appeals and Interferences reverse all standing rejections of claims 20 and 24–40 and remand the case to the Examiner for allowance of all pending claims.

VIII. CLAIMS APPENDIX—37 C.F.R. § 41.37(c)(1)(viii)

A copy of the pending claims involved in this appeal is appended hereto.

IX. EVIDENCE APPENDIX—37 C.F.R. § 41.37(c)(1)(ix)

No evidence has been submitted pursuant to 37 CFR §§ 1.130, 1.131, or 1.132 or entered by the Examiner and relied upon by Appellants in this appeal.

X. RELATED PROCEEDINGS APPENDIX—37 C.F.R. § 41.37(c)(1)(x)

There are no related proceedings.

XI. CONCLUSION

In light of the foregoing arguments, Appellants maintain that the Examiner has failed to establish a *prima facie* case that claims 20 and 24–40 would have been obvious to a person of ordinary skill in the art at the time of the claimed invention. In addition to, or alternatively, even if the Examiner has established a *prima facie* case of obviousness of claims 20 and 24–40 (which Appellants do not hereby admit), Appellants have set forth arguments that rebut a *prima facie* case of obviousness. Accordingly, Appellants respectfully request that the Board of Patent Appeals and Interferences reverse the rejections of claims 20 and 24–40 under 35 U.S.C. § 103(a) and remand the case to the Examiner for allowance of all pending claims.

Respectfully submitted,

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CLAIMS APPENDIX—37 C.F.R. § 41.37(c)(1)(viii)

The claims involved in the Appeal are as follows:

1–19. (Canceled).

20. (Rejected) An enteric soft capsule shell formed from a gel mass composition comprising:

(a) a film-forming, water-soluble polymer,

(b) an acid-insoluble polymer; and

(c) an alkaline aqueous solvent;

wherein the ratio of acid-insoluble polymer to film-forming, water-soluble polymer is from 30:70 to 45:55 by weight;

the final pH of the gel mass is less than or equal to about 9 pH units; and

the moisture content of the enteric soft capsule shell formed from the gel mass composition is from about 2% to about 10%.

21–23. (Canceled).

24. (Rejected) The enteric soft capsule shell of claim 20, wherein the film-forming, water-soluble polymer is proteinaceous.

25. (Rejected) The enteric soft capsule shell of claim 24, wherein the proteinaceous film-forming, water-soluble polymer is gelatin.

26. (Rejected) The enteric soft capsule shell of claim 25, wherein the gelatin is extracted from animal bones or skins, and has about 100 to about 250 blooms.

27. (Rejected) The enteric soft capsule shell of claim 20, wherein the film-forming, water-soluble polymer is a carbohydrate.

28. (Rejected) The enteric soft capsule shell of claim 27, wherein the carbohydrate is selected from the group consisting of hydroxypropyl methylcellulose and methyl cellulose.

29. (Rejected) The enteric soft capsule shell of claim 20, wherein the acid-insoluble polymer is selected from the group consisting of acrylic and methacrylic acid copolymers, cellulose acetate esters such as phthalate, butyrate, hydroxypropyl methyl cellulose phthalate, and salts thereof.

30. (Rejected) The enteric soft capsule shell of claim 20, further comprising at least one plasticizer selected from the group consisting of sorbitol, glycerol, polyethylene glycol, poly-alcohols with 3 to 6 carbon atoms, citric acid, citric acid esters, triethyl citrate, and combinations thereof.

31. (Rejected) The enteric soft capsule shell of claim 20, wherein the alkaline aqueous solvent comprises an alkali selected from the group consisting of ammonia, sodium hydroxide, potassium hydroxide, ethylenediamine, hydroxylamine, and tri-ethanolamine.

32. (Rejected) The enteric soft capsule shell of claim 20, wherein the alkaline aqueous solvent comprises a volatile alkali.

33. (Rejected) The enteric soft capsule shell of claim 32, wherein the volatile alkali is selected from the group consisting of ammonia and ethylenediamine.

34. (Rejected) The enteric soft capsule shell of claim 20, wherein the alkaline aqueous solvent is a hydroalcoholic solution.

35. (Rejected) The enteric soft capsule shell of claim 20, where the final pH of the gel mass is less than or equal to about 8.5.

36. (Rejected) The enteric soft capsule shell of claim 20, wherein the enteric soft capsule shell has a moisture content of from about 2% to about 10%.

37. (Rejected) The enteric soft capsule shell of claim 36, wherein the moisture content is from about 4% to about 8%.

38. (Rejected) The enteric soft capsule shell of claim 36, wherein the moisture content is about 8%.

39. (Rejected) The enteric soft capsule shell of claim 20, wherein the gel mass compositions comprises a plasticizer, and the ratio of plasticizer to film-forming, water-soluble polymer is from about 1:9 to about 1:1 by weight.

40. (Rejected) The enteric soft capsule shell of claim 39, wherein the ratio of plasticizer to film-forming, water-soluble polymer is about 1:3 by weight.

EVIDENCE APPENDIX—37 C.F.R. § 41.37(c)(1)(ix)

No evidence has been submitted pursuant to 37 C.F.R. §§ 1.130, 1.131 or 1.132 or entered by the Examiner and relied upon by Appellants in this appeal.

RELATED PROCEEDINGS APPENDIX—37 C.F.R. § 41.37(c)(1)(x)

None.